

I. AMENDMENTS

In the Specification:

On page 1, after the title, please insert the following statement:

--STATEMENT OF RIGHTS TO INVENTIONS MADE UNDER
FEDERALLY SPONSORED RESEARCH--

31 This invention was made in part during work supported by the U.S. government, including a grant from the National Institutes of Health (NIH) CA61348. The government may have certain rights in the invention.--

On page 4, line 1, please change "Figure 2B" to -- Figure 2C-- as suggested by the Examiner.

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In the Claims:

Please amend claims 1-5, 29-30, 37-43, 45, and 54-55, under the provision of 37 C.F.R. § 1.121(b) by deleting the bracketed material and inserting the underlined material as follows:

1. (Four times Amended) An isolated FADD protein comprising the amino acid sequence shown in SEQ ID NO:2, or an analog [and analogs] thereof having conservative amino acid substitutions and the analog induces [analogues being capable of inducing] apoptosis in a suitable cell or binds to [binding] the cytoplasmic domain of a Fas receptor.

32 2. (Thrice Amended) Purified [mammalian] FADD protein produced by [the process of claim 53] contacting a sample suspected of containing the FADD protein or polypeptide with a protein or polypeptide comprising the cytoplasmic domain of Fas under conditions suitable for the Fas-containing protein or polypeptide to bind the FADD protein or polypeptide to form a complex, and isolating any Fas-FADD complex formed, wherein the purified FADD protein [and characterized in having] has an apparent molecular weight of about 23.3 kDa as determined by an SDS polyacrylamide gel under reducing conditions.

3. (Thrice Amended) A polypeptide fragment of the protein of claim 1, comprising amino acid 24 to amino acid 208 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analog being capable of binding] binds to the cytoplasmic domain of a Fas receptor.

4. (Thrice Amended) A polypeptide fragment of the protein of claim 1, wherein the polypeptide consists of at least the C-terminal portion of the protein, or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analog being capable of binding] binds to the cytoplasmic domain of a Fas receptor.

5. (Thrice Amended) A polypeptide fragment of the protein of claim 1, wherein the polypeptide consists of at least the N-terminal portion of the protein or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analog being capable of inducing] induces apoptosis in a suitable cell.

29. (Twice Amended) A method for screening for an agent that inhibits binding of a FADD protein or polypeptide to [useful to modulate cellular function regulated by] the Fas receptor [pathway], the method comprising the steps of:

a) contacting the agent to be tested with the cytoplasmic domain of the Fas receptor bound to a solid support under conditions favoring binding of the cytoplasmic domain to the FADD protein or polypeptide of claim 54;

b) contacting detectably-labeled FADD protein or polypeptide of claim 54 to the solid support of step a) under conditions favoring binding of Fas cytoplasmic domain receptor to FADD and detecting the presence of any complex formed between the Fas receptor and the detectably-labeled FADD to form Fas receptor-FADD complex, the absence of complex being indicative that the agent inhibits binding of FADD to the Fas receptor[; and

c) analyzing the results of step b) to determine how the agent modulates the cellular function regulated by the Fas receptor pathway].

30. (Twice Amended) A method for screening for an agent that inhibits binding of a FADD protein or polypeptide to [useful to modulate cellular function regulated by] the Fas receptor [pathway], the method comprising the steps of:

a) contacting detectably-labeled FADD protein or polypeptide of claim 54 to a Fas cytoplasmic domain receptor bound to a solid support under conditions favoring binding of the cytoplasmic domain [receptor] to FADD;

3
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b) contacting the agent to be screened with the receptor bound to the support of step a) under conditions favoring binding of the cytoplasmic domain [to] of the receptor to FADD protein or polypeptide of claim 54 and detecting the presence of any complex formed between Fas receptor and the detectably-labeled FADD protein or polypeptide to form Fas receptor-FADD complex, the absence of complex being indicative that the agent competitively inhibits binding of FADD to the Fas receptor[; and

c) analyzing the results of step b) to determine how the agent modulates the cellular function regulated by the Fas receptor pathway].

37. (Twice Amended) A polypeptide fragment of the protein of claim 1, comprising amino acid 41 to amino acid 208 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analogs being capable of binding] binds to the cytoplasmic domain of the Fas receptor.

38. (Twice Amended) A polypeptide fragment of the protein of claim 1, comprising amino acid 111 to amino acid 180 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analogs being capable of binding] binds to the cytoplasmic domain of the Fas receptor.

39. (Twice Amended) A polypeptide fragment of the protein of claim 1, comprising amino acid 35 to amino acid 208 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analogs being capable of binding] binds to the cytoplasmic domain of a Fas receptor.

40. (Twice Amended) A polypeptide fragment of claim 5, comprising amino acid 1 to amino acid 117 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analogs being capable of inducing] induces apoptosis in a suitable cell.

41. (Twice Amended) A polypeptide fragment of the protein of claim 1, comprising amino acid 41 to amino acid 208 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analogs being capable of binding] binds to the cytoplasmic domain of a Fas receptor.

42. (Twice Amended) A polypeptide fragment of the protein of claim 1, comprising amino acid 61 to amino acid 208 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analogs being capable of binding] binds to the cytoplasmic domain of a Fas receptor.

43. (Twice Amended) A polypeptide fragment of the protein of claim 1, comprising amino acid 80 to amino acid 208 or an analog [and analogs] thereof having conservative amino acid substitutions and the analog [analogs being capable of binding] binds to the cytoplasmic domain of a Fas receptor.

45. (Twice Amended) A FADD mutein protein comprising the amino acid sequence shown in SEQ ID NO: 2 and having asparagine at amino acid 121 or an analog [and analogs]

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thereof having conservative amino acid substitutions at amino acids 1 to 120 and 122 to 208 and the analog [analogs being capable of inducing] induces apoptosis in a suitable cell.

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54 (Amended) An isolated FADD polypeptide fragment of the protein of claim 1[, wherein the fragment has the ability to bind] that binds to the cytoplasmic domain of the Fas receptor.

55. (Amended) An isolated FADD polypeptide fragment of the protein of claim 1[, wherein the fragment has the ability to induce] that induces apoptosis in a suitable cell.

Please add new claims 57-60, as follows:

57. (New) A method for screening for an agent of claim 29 or 30, further comprising the step of analyzing the results of step b) to determine how the agent modulates the cellular function regulated by the Fas receptor pathway.

58. (New) A method for screening for an agent useful to modulate a cellular function regulated by FADD, the method comprising the steps of:

37
a) contacting the agent to be tested with a FADD fragment comprising the N-terminal portion of FADD bound to a solid support under conditions favoring binding of the N-terminal portion of FADD to its ligand;

b) detecting the presence of any complex formed between the FADD fragment and the agent, wherein the presence of complex being indicative that the agent binds to the N-terminal portion of FADD; and

c) analyzing the results of step b) to determine how the agent modulates the cellular function regulated by FADD.